PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference REG/G25522WO	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2005/000367	International filing date *(day/month/year)* 03.02.2005	Priority date *(day/month/year)* 03.02.2004
International Patent Classification (IPC) or national classification and IPC G01N33/543		
Applicant SPHERE MEDICAL LTD et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29.11.2005	22.02.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Moreno de Vega, C Telephone No. +49 89 2399-7486

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2005/000367

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-24	as originally filed

Claims, Numbers

9-27	as originally filed
1-8	received on 29.11.2005 with letter of 25.11.2005

Drawings, Sheets

1/6-6/6	as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 25-27 with respect to industrial applicability

because:

☒ the said international application, or the said claims Nos. 25-27 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2005/000367

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-27
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-27
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-24
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No.
PCT/GB2005/000367

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The scope of claims 25-27 encompasses embodiments related to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT (diagnostic methods to be carried out in vivo involving the treatment of the living human/animal body by surgery). Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: WO 2004/027393 A (THE CHARLES STARK DRAPER LABORATORY, INC) 1 April 2004 (2004-04-01)
D2: US 2003/053935 A1 (WILLIAMS JOHN R ET AL) 20 March 2003 (2003-03-20)
D3: US-A-5 910 286 (LIPSKIER ET AL) 8 June 1999 (1999-06-08)
D4: JAKOBY B ET AL: "A novel molecularly imprinted thin film applied to a Love wave gas sensor" SENSORS AND ACTUATORS A, ELSEVIER SEQUOIA S.A., LAUSANNE, CH, vol. 76, no. 1-3, 30 August 1999 (1999-08-30), pages 93-97, XP004184418 ISSN: 0924-4247
D5: WO 00/22425 A (COMMISSARIAT A L'ENERGIE ATOMIQUE; CLERC, JEAN-FREDERIC; CAILLAT, PATR) 20 April 2000 (2000-04-20)
D6: US-B1-6 197 503 (VO-DINH TUAN ET AL) 6 March 2001 (2001-03-06)

2. Documents D1 and D2 disclose a resistive sensor comprising a substrate with two electrochemical systems, each formed by a couple of electrodes deposited and protruding from the substrate, each couple of electrodes limiting an interior space which is filled with a molecular imprinted polymer. In D1 and D2, contrary to the present invention, the electrodes cannot confine the "first interior space" in all directions, as at least one non-conducting gap is required between the electrodes. The confined structure of the present invention confines the polymer/solvent structure. Thus, claims 1-27 are novel over D1 and D2.

3. Documents D3 and D4 disclose piezoelectric acoustic sensors comprising a planar piezoelectric substrate and a molecular imprinted polymer between emitter and receiver electrodes patterned on the planar substrate. These documents do not disclose a confinement structure comprising a first limiting structure defining a first interior space within the meaning of claim 1.

4. Document D5 discloses a microsystem in which an array of microwells is formed on a silicon substrate coated with a metallic layer by deposition of a coating layer of polyimide. The bottom of each well works as working electrode for deposition of a layer of electropolymerized polypirrole. The microwell plate of D5 does not have a transducer proximal to each well. Thus, claims 1-27 are novel over D5.

5. D6 relates to a self-contained DNA biosensor, built up from a number of layers with have previously been fabricated and need to be assembled with great accuracy. In the present invention, the confinement structures are formed directly on the substrate by a deposition process, thereby forming a sensor with a single unitary structure which does not require the difficult assembly of multiple layers. Present claims 1-27 are therefore new over D6.

6. The technical problem to be solved by the present invention is the provision of a sensor capable of functioning in a clinical setting. The solution provided by the present invention has advantages that are not derivable from the known prior art

documents, taken alone or in combination: the confinement structure of the present invention can accurately control the extent of the pool and the volume of the mixture to be deposited into the pool, and allows the creation of sensors in close proximity to each other without any danger of intermixing the functional layers; said structure is also important in the attachment by deposition, improving the stability of the film and avoiding peeling.

For these reasons, it is considered that present claims 1-27 meet the requirements of Article 33(2) and (3) PCT.

Claims

1. A sensor comprising

a substrate;

a confinement structure created from materials applied to the substrate by deposition, wherein the confinement structure comprises at least a first limiting structure defining a first interior space;

a transducer proximal to the first interior space; and

a first synthetic polymer capable of selectively binding a first analyte, within the confinement structure.

2. A sensor as claimed in claim 1, wherein the confinement structure further comprises a second limiting structure defining a second interior space, the second interior space containing the first interior space.

3. A sensor as claimed in claim 2, wherein the confinement structure further comprises one or more further limiting structures defining one or more further interior spaces, the one or more further interior spaces each containing a preceding interior space.

4. A sensor as claimed in any preceding claim, wherein the first synthetic polymer capable of selectively binding a first analyte is disposed in the first interior space.

5. A sensor as claimed in any preceding claim, wherein the first synthetic polymer capable of selectively binding a first analyte is disposed in the second or one or more further interior spaces.

6. A sensor as claimed in any preceding claim, wherein the internal diameter of the first limiting structure is about 10-350 μm.

7. A sensor as claimed in any preceding claim, wherein height of the first limiting structure is about 1-10 μm.

8. A sensor as claimed in any of claims 2 to 7, wherein the internal diameter of the second limiting structure is about 50-600 μm.